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10/506,952	09/08/2004	Celal Albayrak	ABS0006/US	6918
33072	7590	05/29/2009		
KAGAN BINDER, PLLC SUITE 200, MAPLE ISLAND BUILDING 221 MAIN STREET NORTH STILLWATER, MN 55082			EXAMINER AUDET, MAURY A	
			ART UNIT	PAPER NUMBER
			1654	
			MAIL DATE	DELIVERY MODE
			05/29/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/506,952

**Applicant(s)**

ALBAYRAK, CELAL

**Examiner**

MAURY AUDET

**Art Unit**

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 2/26/09.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 3-9 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SE/US)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's response and Notice of Appeal is acknowledged. Following the Appeal Conference roundtable, it was determined that there was insufficient suggestion/motivation to uphold a prima facie case of obviousness under 35 USC 103. Thus, prosecution has been re-opened. Based on the updated search of the art directed to the gap in the suggestion/motivation statement under the previous 103 reasoning, additional prior art of record is now recited in combination with the previous art of record, in order to better solidify the suggestion/motivation reasoning that it would have been obvious for one of ordinary skill in the art at the time of the invention to arrive at the present invention, as claimed.

Additionally, following a closer review of the claimed invention, certain claim limitations are now viewed as raising issues of indefiniteness, which have been raised under 35 USC 112 2<sup>nd</sup>, and must be addressed either by amendment where support may be found to more distinctly claim the invention and/or argument.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 3-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hutchinson (US 5,889,110) in view of Barry et al. (US 2004/0126900 A1), Chen et al. (US 7,081,489), Bhagwatwar et al. (US 20030049320) and Yeh et al. (US 5869103, cited by International Authority in related PCT Search Report).

**As noted in the previous action:**

Applicant's arguments have been considered but are not found persuasive. Specifically, even after Chen et al. was cited, Applicant argues that the combination of references does not teach a method of carrying out the process in solution; and that the active substance is not precipitated in the polymer solution prior to solidifying the polymer. Applicant's arguments have been fully considered, but even if not expressly taught, as the Examiner has concluded, and in light of what the skilled artisan was well versed in, the aforementioned form/sequence of arriving at the same end product, absent a clear unexpected result, would have merely been a matter of routine optimization by one of ordinary skill in the art, to arrive at, absent more convincing evidence to the contrary. Applicant argues that the combination of references does

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not teach the precipitation of the active substance prior to solidification. Chen et al. is cited to remedy this deficiency, while falling within analogous art to Hutchinson and providing motivation to arrive at the claimed invention.

**The modified rejection to include Barry et al. is below:**

Barry et al. teach the use of  $> 1$  solvent, and precipitating nanoparticles, in solution:

[0089] As far as reaction conditions are concerned, it is preferable to functionalize the nanoparticle in an aqueous system. The surfactants and the oil phase, residual from the synthesis of the nanoparticle core, can be removed through the use (singularly **or in combination**) of ~~solvent~~ **washing, for instance using ethanol to solubilize the surfactant and oil while precipitating the polymer nanoparticles**; surfactant-adsorbing beads; dialysis; or the use of aqueous systems such as 4M urea. **Methods for surfactant removal are known in the art.**

Hutchinson was discussed previously (see entire document). Due to the present claims amorphous language, it is still unclear whether the steps of Hutchinson, in various examples, expressly teach the "effecting precipitation" step as comprising an L 1/L2 combination wherein the latter is increased over the former (Applicant's claims 2-4). It is clear Hutchinson teach L1/L2, wherein the latter is increased, following a precipitation step, and wherein the L2 is a non-solvent to the goserelin acetate (see e.g. claim 16, step iv)). This seems to be the only issue, as to whether Hutchinson expressly teaches within one of the examples this stepwise approach, or whether such would have been merely obvious. Additionally, it is not clear whether Hutchinson teach volume fraction of the aqueous surfactant solution ranges between 60 and 80% of the aqueous and organic solvents combined in step (b) (Applicant's claim 7).

As previously discussed, Chen et al. teach making of polymeric nanoparticles comprises providing active agent nanoparticles having average diameter of 5-100 nm. The active agent nanoparticles are treated with an anionic surfactant to form modified active agent nanoparticles. The modified nanoactive agent nanoparticles are mixed with a solution of polymer in a *solvent at first temperature*, which is greater than the melting temperature of the polymer and less than boiling point of the *solvent to form a first mixture*. The mixing comprises the use of sonication. A *non-solvent* is mixed with *first mixture to form a second mixture*. The second mixture is sonicated to form an emulsion. The emulsion is cooled to a *second temperature at a rate effective to precipitate polymeric nanoparticles* comprising the polymer with the modified active agent nanoparticles (abstract, entire document).

As previously discussed, Bhagwatwar et al teach a method of forming microparticles comprising the elected species of active substance goserelin acetate and polymer poly-DL-lactide-co-glycolide (e.g. para 158, claims 8, 26, 37, and 47), with any suitable solution/solvent well known in the art (e.g. para 2-5, 40, 75, entire document), and contemplating any Well known microparticle size well known in the art for the use of microparticles in vivo. Bhagwatwar et al. teach microparticles, but does not expressly teach that microparticles includes the species nanoparticles and specific size ranges under 1  $\mu\text{m}$ , was not expressly found therein (e.g. Applicant's claim 11).

As previously discussed, Yeh et al. teach the formation of nano/microparticle, which comprises active substances and the polymer poly-DL-lactide-co-glycolide, including in size ranges less than 1  $\mu\text{m}$  (e.g. col. 1, col. 3, lines 35-41, entire document).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to arrive at an L1/L2 solvent mixture as part of the "effecting precipitation" step, in Hutchinson, because Barry et al. advantageously teaches a water (L1) and oil (L2) solvent mixture that precipitates the active agent in solution. Barry et al. also points out that the solution can also be removed, "as well known in the art" - indicating this is an old art and well-versed in routine optimization. Chen et al. advantageously teach that the active substance is not added in solid state to the polymer solution and is formed in situ and precipitated as part of the solvent process. Hutchinson, within the analogous art, advantageously teach various steps and means of carrying out the same ultimate goal of microparticle formation comprising active substance goserelin acetate within polymer poly-DL-lactide-co-glycolide, and further in view of the advantageous teachings of Barry et al., Chen et al., as well as Bhagwatwar et al., using different steps to carry out the same and Yeh et al. to arrive at size limitations within that contemplated herein.

Likewise, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a volume fraction of the aqueous surfactant solution ranges between 60 and 80% of the aqueous and organic solvents in the initial mixing of the goserelin acetate-polymer poly-DL-lactide-co-glycolide of Hutchinson, in view of Barry et al., Chen et al., and further in view of Bhagwatwar et al. or Yeh et al., because both Hutchinson and Chen et al. advantageously teach routinely optimizable amounts of the solutions/solvents therein, as do the latter references, to carry out the desired results of the artisan and the selection of the aqueous surfactant solution ranges between 60 and 80% of the aqueous and organic solvents in the initial mixing of the goserelin acetate-polymer poly-DL-lactide-co-glycolide, would have merely obvious depending on the results sought, absence evidence to the contrary.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

***Claim Rejections - 35 USC § 112 2nd***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In e.g. claim 1, the term solvent is indefinite, as to L1 and L2, alone as well as in comparison to each other. Is L1 an inorganic solvent...if L2 is an "organic" solvent? If not, can L1 and L2 be the same solvent? What solvents under each then, contemplate the metes and bounds of the invention? It is suggested that applicant claim the solvents based on Markush-type claiming (e.g. L2 is selected from the group of organic solvents consisting of...).

In e.g. claim 1, what is meant by polymer? The metes and bounds of what may constitute the polymer are undefined, other than claim 9, to poly(DL-lactide-co-glycolide). Like L1 & L2, it is suggested that Applicant consider claiming the polymer in Markush fashion or amend claim 9 in to base claim 1.

In e.g. claim 1, what is meant by active agent? The metes and bounds are undefined. Can any L1 or any L2 precipitate ANY active agent? If so, the metes and bounds of the claim,



read in light of the specification, have not so conveyed. The only active agent disclosed by claim is that of peptides and proteins. If this is the metes and bounds of what can be precipitated in situ via the L1/L2 stepwise preparation of nano-/micoparticles containing said peptides/proteins, than Applicant should consider amending claim 8 in to the base claim 1, or claiming the active group via Markush style.

### *Conclusion*

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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MA, 5/9/2009

/Maury Audet/

Examiner, Art Unit 1654

/Cecilia Tsang/

Supervisory Patent Examiner, Art Unit 1654